DANGEROUS OMISSIONS:
The consequences of ignoring decision uncertainty

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Introduction

When determining which technologies to reimburse within a health care system there are two conceptually distinct but simultaneous decisions:

1) Should a technology be adopted given the existing evidence (and the current uncertainty)?

2) Is additional evidence required to support the adoption decision?

Overview

• Decision theory

• The policy environment

• Decision rules incorporating the opportunity losses of adoption and rejection

• Incorporating uncertainty

• Discussion and Conclusions
Decision theory and value of information
Decision-making with uncertainty

• The decision to adopt a technology
  – Objective of health care system
    • Maximise health subject to budget constraint
  – Cost-effectiveness analysis
    • Compare health gained with new intervention to health displaced in transferring resources from existing programmes

• The decision to acquire more evidence
  – Value of information
    • Compare value of reducing expected cost of uncertainty to health displaced by allocating resources to research
The adoption decision

• Objective: maximise health gains from available resources
  – Simplifying conditions: absence of irreversibility and sunk costs
    (Palmer and Smith 2002, Eckermann and Willan 2008)

Decision to adopt technology, $j$, depends on
  – expected cost, $C_j$
  – expected outcomes, $Q_j$
  – cost-effectiveness threshold, $\lambda$

Net benefit framework: $NB_j = Q_j - C_j/\lambda$
Assume NB is function of uncertain parameters, $\theta$
The irrelevance of inference

• Decision made before it is known how uncertain parameters in the model, $\theta$, resolve.
• With current information should adopt technology that maximises expected NB

$$\max_j E_\theta NB(j, \theta)$$

• Failure to adopt simply because differences in NB are not regarded as statistically significant will impose opportunity costs on patients who could benefit
However....

• Making decisions on expected NB does not mean that uncertainty is irrelevant

• The second question of whether additional evidence is required must be addressed, otherwise:
  – decisions made on limited evidence
  – decisions made on poor quality evidence
The decision to acquire more evidence

• Same objective and conditions as adoption decision
• With decision uncertainty, the technology selected on current evidence may not have maximum NB
  – In these cases patients forgo potential health gains
  – In absence of uncertainty, could always pick technology that maximised health

Expected value of perfect information (EVPI)
  – Difference between expected NB of the decision made with perfect information about $\Theta$, and the decision made with current information
Expected Value of Perfect Information

• With perfect information can select technology that maximises NB for a particular value of $\theta$
  – true values of $\theta$ are unknown

• Expected value of decision with perfect info found by averaging maximum NB over the joint distribution of $\theta$:

$$ E\left( NB^{**} \right) = E_{\theta} \max_{j} NB\left( j, \theta \right) $$

• EVPI is difference between this and expected NB of decision with current info
Population EVPI (and NB)

- Information has public good characteristics
- EVPI for the population based on:
  - Effective lifetime of technology, $T$
  - Incidence over this period, $I_t$
  - Discount rate, $r$

$$\text{EVPI}_{\text{pop}} = \text{EVPI} \cdot \sum_{t=1}^{T} \frac{I_t}{(1 + r)^t}$$

- Population EVPI provides upper bound for value of additional research
  - Provides necessary condition for additional research
  - $\text{EVPI}_{\text{pop}}$ must exceed costs of further investigation
The policy environment
Background

• Economic evaluation increasingly used to inform reimbursement/adoption decisions made by funders of health care
  – For example

UK  Canada  Australia  Sweden
The policy environment

- Institutions with remit for making adoption decisions often separated from those responsible for prioritising and commissioning research
  - cannot directly arrange funding for research
  - cannot issue/enforce conditional approval

- In these circumstances the adoption decision is the only policy instrument available
  - not clear that question of whether further evidence needed is being addressed simultaneously and consistently
Expected NB decision-making

• Decisions can continue to be based on expected NB if the prospects of further research are unaffected by the adoption decision

• However this is unlikely because:
  – adoption removes incentives for manufacturer of technology to conduct further research
  – diffusion of technology, particularly when mandatory, means future clinical trials less likely to be supported or regarded as ethical
  – adoption can damage recruitment to ongoing trials
Implications

• Adoption can remove an option to acquire additional evidence

• The opportunity loss of adopting a technology can be measured by the value of information that may be forgone
  – this opportunity loss could be greater than the net benefits offered by the technology

• If reimbursement authorities are not given remit to commission/demand research then may be better to deny approval of apparently cost-effective technology
Calculating the opportunity losses of adoption and rejection
Context

- Decision maker whose role is limited to granting approval for reimbursement of mutually exclusive alternatives, \( j \)
- New technology, \( j^* \), has greater expected NB than current practice, \( j_0 \)

- To estimate value of information forgone need assessments of:
  - Probability that research will be conducted, \( \alpha \)
  - Time at which research will report, \( \tau \)
Population to benefit

• Split future patient population into
  – Those who benefit from treatment decision based on current evidence:
    \[ P_{t<\tau} = \sum_{t=1}^{\tau} \frac{I_t}{(1+r)^t} \]
  – Those who can benefit from decision incorporating results from further research:
    \[ P_{t>\tau} = \sum_{t=\tau}^{T} \frac{I_t}{(1+r)^t} \]
Expected net benefits of rejection

• If approval of $j^*$ is withheld, patients receive $j_0$ and the associated NB, $E_\theta NB(j_0, \theta)$

• If research conducted and reports at time, $\tau$, decision can be revised and the maximum future patients will receive is $E_\theta \max_j NB(j, \theta)$:

• The expected net benefits of rejecting $j^*$ are then:

$$
B_R = E\left(NB_{j^0}\right) \cdot P_{t<\tau} + (1 - \alpha_R) \cdot E\left(NB_{j^0}\right) \cdot P_{t>\tau} + \alpha_R \cdot E\left(NB^{**}\right) \cdot P_{t>\tau}
$$
Expected net benefits of adoption

- Patients receive \( j^* \) and the associated net benefits, \( E_\theta \text{NB}(j^*, \theta) \)

- If research conducted and reports at time, \( \tau \), decision can be revised and the maximum future patients will receive is \( E_\theta \max_j \text{NB}(j, \theta) \):

- The expected net benefits of adopting \( j^* \) are then:

\[
B_A = E\left(NB_{j^*}\right) \cdot P_{t<\tau} + (1 - \alpha_A) \cdot E\left(NB_{j^*}\right) \cdot P_{t>\tau} + \alpha_A \cdot E\left(NB^{**}\right) \cdot P_{t>\tau}
\]
Condition for immediate adoption

- Benefits of adoption should exceed benefits of reject:

$$B_A - B_R = \left[ E(NB_{j*}) - E(NB_{j^0}) \right] (P_{t<\tau} + (1-\alpha_R) P_{t>\tau}) - (\alpha_R - \alpha_A) \left[ E(NB^{**}) - E(NB_{j^*}) \right] P_{t>\tau}$$

- Standard condition for adoption is special case
  - Adoption does not affect prospects for research, $\alpha_A = \alpha_R$
  - Approve if $E(NB_{j^*}) \geq E(NB_{j^0})$
New decision rule
Examples

• Will now demonstrate:
  – Difference with decision making based on expected NB
  – Incentives offered by decision rule that incorporates opportunity cost of research forgone
    • Price
    • Uncertainty
  – Implications for different types of research
\[ \alpha_R = 1 \quad \alpha_A = 0 \quad \tau = 2 \]
Combinations of $\alpha_R$ and $\tau$ for which $B_A = B_R$

- Approve based on current evidence
- Reject?

$sufficient$ $condition$

$\lambda = £30,000$

$\alpha_A = 0$
The decision to adopt

- Technologies for which research prospects lie to the north-east of the boundary should be approved
- Technologies that lie to the south-west may require further consideration
- Boundary based on value of perfect info
  - Boundary based on sample info lies to south-west
  - Computationally expensive to assess EVSI
  - However, given $\alpha$ and $\tau$ can calculate threshold for EVSI as a guide
Impact of the threshold on the boundary for approval

\[
\lambda = £25k = \text{ICER}
\]

\[
\lambda = £26,000
\]

\[
\lambda = £27,000
\]

\[
\lambda = £30,000
\]

\[
\lambda = £45,000
\]
Impact of the price and uncertainty on the boundary for approval

- **Time research reports** ($\tau$)
- **Probability of research** ($\alpha_R$)

**Original boundary**

- $\alpha_R=0.8, \tau=2$

**Reduce price or uncertainty**

- $\alpha=0.8, \tau=2$
Impact of price and uncertainty

• Reducing price increases the benefits of immediate adoption, $E_0 \cdot NB(j^*, \theta)$
  – If uncertainty associated with incremental cost, reducing price also reduces value of information

• Reducing uncertainty reduces the value of any information forgone by immediate adoption

• Reducing price or uncertainty will in most cases increase $B_A - B_R$
Incentives to manufacturers

To review:

- Decision rules based solely on expected NB
  - set price so that ICER just below threshold
  - thus minimising R&D costs and capturing surplus

- Decision rules that consider the opportunity loss of adoption
  - provide more evidence to support technology
  - reduce price
What type of research?
Research decision space

• Different parameters contribute to overall decision uncertainty
  – Type of evidence determines appropriate research design
  – Different research designs affected in different ways by adoption

• Suppose $\theta_1, \theta_2 \cup \theta$
  – If $\theta_1$ relative effect of $j^*$ → RCT; $\alpha_{R}^{\theta_1} > \alpha_{A}^{\theta_1} = 0$
  – If $\theta_2$ quality of life → observational study; $\alpha_{R}^{\theta_2} = \alpha_{A}^{\theta_2}$
  – Time to research $\tau_{\theta_1} > \tau_{\theta_2}$
Uncertainty in $\alpha$ and $\tau$

- Characterise uncertainty associated with $\tau$ and $\alpha$ by assigning appropriate prior distributions
  - allows calculation of expected payoff from immediate adoption, $E(\Pi_A)$

- For example:
  - trial registry indicates ongoing trial
  - protocol indicates when results expected to be reported
    $\tau \sim \text{gamma}(25,0.1); \quad \alpha \sim \text{beta}(2.4,0.6)$

  - no information about potential further research
    $\tau \sim \text{unif}(0,T); \quad \alpha \sim \text{unif}(0,1)$
Figure 5. Expected net benefits of immediate adoption

- Uniform priors
- Informative priors
Discussion
Recap

• If objective is to maximise health gains from available resources
  – has been argued that decision to adopt be based on expected cost, expected outcomes and an assessment of the cost-effectiveness threshold

• However this is only justified
  – if question of whether additional evidence required assessed simultaneously
  – or adoption decision does not affect prospects for future research
Recap

• Adoption decision is likely to affect prospects for further research
  – adoption decision cannot be separated from question of whether evidence is sufficient
  – not clear whether this is recognised in current policy environment

• Where adoption decision only policy instrument
  – adoption decision cannot be based on expected NB
  – require assessment of opportunity loss of immediate adoption
Benefits of formal approach

• Have demonstrated formal framework for evaluating the opportunity losses
  – provides incentives for manufacturers to reduce price or provide additional evidence

• Current ‘informal’ approach
  – lack of legal standing to back-up recommendations
  – not transparent
    • problems with consistency, predictability, incentives
Other issues

• Rely on EVPI and assessment of threshold for EVSI

• Consider only current decision problem
  – value of additional information may be underestimated